UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,574	10/28/2003	Denis Barritault	1003-DIV-01	4857

35811 7590 07/05/2005

IP GROUP OF DLA PIPER RUDNICK GRAY CARY US LLP
1650 MARKET ST
SUITE 4900
PHILADELPHIA, PA 19103

EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 07/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/695,574	BARRITAULT ET AL.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42 and 61-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42 and 61-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *May 2, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed May 2, 2005, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 42 and 61-64 are pending and are presented for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 64 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the claim recites "a process for **reducing fibroses**...", though the specification as filed contains no such limitation. The asserted support for the limitation lies in statements that the different RGTA restores almost exactly the control behavior of HISM cells (page 56, lines 13-21). However, this does not expressly disclose that different RGTA reduce fibroses. In sum, because the specification as filed fails to provide clear support for the new claim language, a new matter rejection is clearly proper.

Claims 42 and 61-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the *in vitro* use of RGTA 1005, 1010, 1012, 1013, 1112,

and 1113 for treating **factors involved in fibroses**, does not reasonably provide enablement for treating fibroses with all other AXY polymers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Regarding undue experimentation, *In re Wands*, 8 USPQ2d 1400, at 1404 (Fed. Cir. 1988) states:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. (Citations omitted).

The rejected claims are drawn to the method of treating and reducing fibroses (including fibroses of smooth muscle and mesenchymal tissues) by administering a pharmaceutical composition comprising the AXY polymer. The claims are broad enough to encompass an infinite number of polymers, of which experimentation would be required for every single variant to determine their efficacy as antifibrotic agents. The specification as filed only provides methods of making polysaccharide polymers, such as carboxymethyl dextran sulfates. More specifically, by applicants' own admission (page 7, last paragraph of Remarks), the specification teaches how to synthesize AXY polymers wherein A is –(O-CH_2-CH_2-CO)- or glucose (not any sugar), and X is –COOH or –COO^- Na^+, and not any and all –R-COO-R' as recited in claims 42 and 64. When A is -(O-CH_2-CH_2-CO)-, the specification teaches only the synthesis of such a polymer wherein Y is –CO-CH_2-CHOH-CH_2-SO_3H or –CO-CH_2-CHOH-CH_2-SO_3-Na^+, not any and all

formulas recited in the claims. Additionally, when A is glucose, the specification only teaches the synthesis of such a polymer wherein Y is $-SO_3H$ or $-SO_3^-Na^+$.

Applicants submit that one skilled in the art, following the teaching of the application, would produce AXY polymers falling within the scope of the claims. Applicants refer to the Petit et al. study (J. Biomacromolecules, 2004, 5(2): 445-52), as an example of a study where AXY polymers were synthesized which had tissue regenerating activities in a rat *in vivo* model. However, at the time the application was filed, the specification had not supplied any evidence that a polymer, such as the polymers of the Petit study, is effective in treating or reducing fibroses. Despite the support provided by the reference, the invention must have been enabling at the time of filing. Moreover, the Petit reference speaks on the tissue regenerating activities of the polymers, not their efficacy in treating or reducing fibroses.

While applicants note that the specification teaches how the claimed AXY polymers are administered *in vivo* to treat fibroses, the matter at hand is whether the polymers are effective in treating and reducing fibroses. The amount of direction provided in the specification speaks only on the *in vitro* administration of polymers of the series RGTA 1000-1025 and 1110-1115 to observe their effect on growth kinetics in smooth muscle tissue cultures, as well as the synthesis of collagens. The specification does not provide actual guidance or evidence supporting the use of the AXY polymer in treating or reducing fibroses (including fibroses of smooth muscle and mesenchymal tissues) in humans or animal models.

Applicants point to several post-filing publications to show that the claimed AXY polymers can be used to treat or reduce fibrosis. The first publication, the Desgranges study, does not teach the claimed AXY polymer, as carboxylmethyl benzylamide sulfonate dextran comprises benzylamine sulfonate, which is excluded from inclusion in AXY polymer as recited in claims 42 and 64. Likewise, the Yamauchi and Alexakis references each disclose polymers (RGTA11 and RG1192) for treating/reducing fibroses which are not AXY polymers as they include benzylamine or benzylamine sulfonate. Furthermore, the Alexakis reference teaches the treatment of intestinal fibrosis, but does not teach the treatment of any and all types of fibrosis.

Applicant's reference to the Desgranges et al., Yamauchi et al., and Alexakis et al. references (pages 8 and 9 of Remarks), all of which were published after the time of the instant invention, is confusing. The standard for determining enablement is whether the person of ordinary skill in the art would have had a reasonable expectation of success in making or using the claimed invention without extensive experimentation at the time the invention was made. Applicant's reference to art made available after the filing date of the instant application does not remedy the deficiencies of the specification as it pertains to the claimed treatment methods.

Indeed, applicant's reference to these post-filing references only affirm the examiner's conclusion that **at the time the instant invention was made**, the skilled artisan would not have had a reasonable expectation of success in using the recited AXY polymers to treat fibrosis, because such treatment has not been reported in the art, even years later. The Alexakis et al. reference, which is the only cited reference that teaches any use of the product **as claimed**, is drawn to *ex vivo* experiments on intestinal tissue, which are not enabling for treatment of fibrosis

in a patient *per se*. In short, even years after the time of filing, skilled artisans have not reached consensus as to a potential treatment for fibrosis comprising the administration of AXY polymers.

In sum, a skilled artisan would have expected to have had to engage in an essentially trial and error process, with little guidance from the specification as filed, to determine suitable AXY polymers which treat and reduce every type of fibrosis. Such a trial and error process clearly constitutes undue experimentation.

Claims 42 and 61-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sough, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117 of *Vas-Cath*) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision all variations of the AXY polymer allowable, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of synthesis of all AXY polymers. Adequate written description requires more than a mere

statement that it is a part of the invention and a set of methods for producing one set of polymers with a specific monomer. The compounds themselves are required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Therefore, only the use of polymers following the synthesis methods as described in the specification (example, the first dextran carboxymethylation step addressed on page 30), but not the full breadth of the claims meet the written description provision of 35 U.S.C §112, first paragraph. More specifically, only synthesis methods are provided AXY polymers wherein A is –(O-CH_2-CH_2-CO), X is –COOH or –COO^-Na^+, and Y is –CO-CH_2-CHOH-CH_2-SO_3H or –CO-CH_2-CHOH-CH_2-$SO_3^-Na^+$, or A is a glucose, X is –COOH or –COO^-Na^+, and Y is –SO_3H or –$SO_3^-Na^+$. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42 and 61-64 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 42 and 64 are indefinite because each recites –(O-CH_2-CH_2-CO)$^-$. It is not clear what is defined by this monomer, as it is not clear whether the last O is double bonded to the last C. Thus, claims 42 and 61-64 are rejected under 35 U.S.C. 112, second paragraph.

Claim 64 is rendered indefinite by the phrase, "reducing fibroses". It is not clear what would constitute a reduction fibroses. For example, reduction of fibroses could be interpreted as meaning the reduction in the quantity of fibroses. Thus, claim 64 is rejected under 35 U.S.C. 112, second paragraph.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan E. Fernandez
Assistant Examiner
Art Unit 1651

sef

FRANCISCO PRATS
PRIMARY EXAMINER